

**IN THE CLAIMS:**

This listing of claims replaces all prior versions, and listings, of claims in the application:

1. (Previously presented) A recombinant retroviral vector comprising a nucleic acid construct, the nucleic acid construct comprising:

a) at least one glucose responsive protein 78 (grp78) non-coding regulatory sequence comprising at least two endoplasmic reticulum stress elements (ERSE) as set forth in SEQ ID NO:1; and

b) a heterologous nucleic acid sequence operatively linked to the regulatory sequence, wherein the heterologous sequence comprises a structural gene that encodes a biologically active protein that converts a non-therapeutically effective compound to a therapeutically-effective compound in vivo.

2. (Previously presented) The vector of claim 1, wherein the glucose responsive protein 78 non-coding regulatory sequence is derived from a mammal.

3. (Currently Amended) The vector of claim 2, wherein the mammal is a rat or a human.

4. (Previously presented) The vector of claim 1, wherein the non-coding regulatory sequence comprises a transcriptional and translational initiation region.

5. (Previously presented) The vector of claim 4, further comprising a transcriptional termination region functional in an animal cell.

6. (Previously presented) The vector of claim 3, wherein the rat non-coding sequence comprises a sequence from about 520 base pairs 5' of the site of initiation of transcription of the rat glucose responsive protein 78 (grp78) coding sequence to about 175 base pairs 3' of the site of initiation of the grp78 coding sequence.

7. (Previously presented) The vector of claim 6, wherein the biologically active protein is an enzyme.

8. (Previously presented) The vector of claim 7, wherein the enzyme is selected from the group consisting of HSV thymidine kinase, VSV thymidine kinase, deoxycytidine kinase, cytosine deaminase and nucleoside phosphorylase.

9. (Previously presented) The vector of claim 1, wherein the non-therapeutically effective compound is selected from the group

consisting of ganciclovir, acyclovir, 6-methoxypurine arabinoside (Ara-M), cytosine arabinoside or cytarabine (Ara-C), fludarabine, 2-chlorodeoxyadenosine, difluorodeoxycytidine, 5-fluorocytidine and 6-methylpurine-2'-deoxyriboside (MeP-dr).

10. (Withdrawn) The nucleic acid construct of claim 1, wherein the therapeutic agent is antisense RNA for disrupting expression of an endogenous coding sequence.

11. (Withdrawn) The nucleic acid construct of claim 10, wherein the endogenous coding sequence is an oncogene.

12. (Withdrawn) The nucleic acid construct of claim 11, wherein the oncogene is selected from the group consisting of ABL, ERBB-1, ERBB-2 (NEU), GIP, GSP, MYC, L-MYC, N-MYC, H-RAS, RET, ROS, K-SAM, SIS, SRC, C-FOS, C-JUN, PRAD1 AND TRK.

13. (Withdrawn) The nucleic acid construct of claim 1, wherein the therapeutic agent is a tumor suppressor protein, or biologically active fragment thereof.

14. (Withdrawn) The nucleic acid construct of claim 13, wherein the tumor suppressor protein, or biologically active fragment thereof, is selected from the group consisting of p53, RB, WT1 (Wilms Tumor) and NF1 (neurofibramatosis).

15. (Previously presented) The vector of claim 1, wherein the cell proliferative disorder is a neoplastic disorder.

16. (Previously presented) The vector of claim 1, wherein the cell proliferative disorder is associated with inflammation.

17. (Withdrawn) A nucleic acid construct comprising: at least one stress-responsive non-coding regulatory sequence comprising at least two endoplasmic reticulum stress elements (ERSE) as set forth in SEQ ID NO:1; and a heterologous nucleic acid sequence operatively linked to the regulatory sequence, wherein expression of the heterologous sequence is regulated by the non-coding sequence and wherein the heterologous sequence encodes a detectable marker.

18. (Withdrawn) The nucleic acid construct of claim 17, wherein the detectable marker is a visually detectable marker.

19. (Withdrawn) The nucleic acid construct of claim 18, wherein the visually detectable marker is green fluorescent protein (GFP), or biologically active derivative thereof.

20. (Withdrawn) The nucleic acid construct of claim 17, wherein the detectable marker is a biologically active protein.

21. (Withdrawn) The nucleic acid construct of claim 20, wherein the biologically active protein is an enzyme.

Claims 22-29. (Canceled)

30. (Previously presented) The vector of claim 1 ~~28~~, wherein the retroviral vector is designated G1NaGRPTK.

31. (Previously presented) A pharmaceutical composition comprising the vector of claim 1 in a pharmaceutically acceptable carrier.

32. (Original) The pharmaceutical composition of claim 31 in a controlled release formulation.

33. (Original) The pharmaceutical composition of claim 31 in a liposomal formulation.

34. (Original) The pharmaceutical composition of claim 31 in a lyophilized form.

35. (Original) The pharmaceutical composition of claim 31 in a unit dose form.

36. (Canceled)

37. (Currently Amended) A method for inhibiting cell proliferation associated with glucose starvation comprising:

a) transducing a target cell capable of cell proliferation with a vector of claim 1, ~~claim 63 or claim 64~~ or claim 63;

b) activating the glucose responsive protein 78 (grp78) non-coding regulatory sequence such that the heterologous nucleic acid sequence comprising a structural gene that encodes a biologically active protein is expressed; and

c) contacting the cell with a non-therapeutically effective compound that is subsequently converted to a therapeutically-effective compound by the biologically active protein,

wherein the therapeutically effective compound inhibits cell proliferation associated with glucose starvation.

38. (Currently Amended) A method for ~~treating~~ reducing a cell proliferative disorder associated with glucose starvation in a subject comprising:

a) locally administering to the subject a vector of claim 1, ~~claim 63 or claim 64~~ or claim 63.

b) transducing a target cell in the subject with a vector of a);

c) activating the glucose responsive protein 78 (grp78) non-coding regulatory sequence such that the heterologous nucleic acid sequence comprising a structural gene that encodes a biologically active protein is expressed; and

d) contacting the cell with a non-therapeutically effective compound that is subsequently converted to a therapeutically-effective compound by the biologically active protein,

wherein the therapeutically effective compound inhibits cell proliferation associated with glucose starvation thereby treating the cell proliferative disorder.

39. (Previously presented) The method of claim 38, wherein the subject is a mammal.

40. (Original) The method of claim 39, wherein the mammal is a mouse.

41. (Original) The method of claim 39, wherein the mammal is a human.

42. (Original) The method of claims 38, wherein the administration is by in vivo administration.

43. (Currently Amended) The method of claim 42, wherein the in vivo administration is by ~~systemic or local~~ direct administration.

44. (Withdrawn) The method of claims 38, wherein the administration is by ex vivo administration.

45. (Previously presented) The method of claim 38, wherein the cell proliferative disorder is a neoplastic disorder.

46. (Original) The method of claim 45, wherein the neoplastic disorder is selected from the group consisting of lung cancer, colon-rectum cancer, breast cancer, prostate cancer, urinary tract cancer, uterine cancer lymphoma, oral cancer, pancreatic cancer, leukemia, melanoma, stomach cancer, thyroid cancer, liver cancer, and brain cancer and ovarian cancer.

47. (Withdrawn) A method for detecting a cell proliferative disorder in a subject comprising administering to the subject a nucleic acid construct of claim 17.

48. (Withdrawn) A transgenic non-human animal comprising a nucleic acid construct according to claim 1, claim 17 or claim 22.



49. (Withdrawn) A transgenic cell comprising a nucleic acid construct according to claim 1, claim 17 or claim 22.

50. (Withdrawn) A transgenic non-human animal having a phenotype characterized by expression of a heterologous nucleic acid sequence encoding a detectable marker otherwise not naturally occurring in the animal, the phenotype being conferred by a transgene contained in the somatic and germ cells of the animal, the transgene comprising the heterologous nucleic acid sequence operably associated with at least one stress-responsive non-coding regulatory sequence comprising at least two endoplasmic reticulum stress elements (ERSE) as set forth in SEQ ID NO:1.

51. (Withdrawn) The transgenic non-human animal of claim 50, wherein the non-coding regulatory sequence is derived from the glucose responsive protein 78 (grp78) promoter sequence.

52. (Withdrawn) The transgenic non-human animal of claim 51, wherein the glucose responsive protein 78 (grp78) promoter sequence comprises a sequence from about 3000 base pairs 5' of the site of initiation of transcription of the grp78 coding sequence to 200 base pairs 3' of the site of initiation of the grp78 coding sequence.

53. (Withdrawn) The transgenic non-human animal of claim 50, wherein the non-coding regulatory sequence comprises a transcriptional and translational initiation region.

54. (Withdrawn) The transgenic non-human animal of claim 50, further comprising a transcriptional termination region functional in an animal cell.

55. (Withdrawn) The transgenic non-human animal of claim 50, wherein the animal is a mammal.

56. (Withdrawn) The transgenic non-human animal of claim 55, wherein the mammal is a mouse.

57. (Withdrawn) A transgenic non-human animal having a phenotype characterized by expression of a heterologous nucleic acid sequence encoding a therapeutic agent effective for treating a cell proliferative disorder otherwise not naturally occurring in the animal, the phenotype being conferred by a transgene contained in the somatic and germ cells of the animal, the transgene comprising the heterologous nucleic acid sequence operably associated with at least one stress-responsive non-coding regulatory sequence comprising at least two endoplasmic reticulum stress elements (ERSE) as set forth in SEQ ID NO:1.

58. (Withdrawn) A method for producing a transgenic non-human animal having a phenotype characterized by expression of a heterologous nucleic acid sequence encoding a detectable marker otherwise not naturally occurring in the animal, wherein said heterologous nucleic acid sequence is operably associated with at least one stress-responsive non-coding regulatory sequence comprising at least two endoplasmic reticulum stress elements (ERSE) as set forth in SEQ ID NO:1, the method comprising:

- a) introducing at least one transgene into a embryo of an animal, the transgene comprising at least one stress-responsive non-coding regulatory sequence comprising at least two endoplasmic reticulum stress elements (ERSE) as set forth in SEQ ID NO:1 isolated upstream from the heterologous nucleic acid sequence encoding a detectable marker;
- b) transplanting the embryo into a pseudopregnant animal;
- c) allowing the embryo to develop to term; and
- d) identifying at least one transgenic offspring containing the transgene.

59. (Withdrawn) The method of claim 58, wherein the introducing of the transgene into the embryo is by introducing an embryonic stem cell containing the transgene into the embryo.

60. (Withdrawn) The method of claim 58, wherein the introducing of the transgene into the embryo is by infecting the embryo with a retrovirus containing the transgene.

61. (Withdrawn) The method of claim 58, wherein the transgenic non-human animal is a mammal.

62. (Withdrawn) The method of claim 61, wherein the mammal is a mouse.

63. (Previously presented) A recombinant retroviral vector comprising a nucleic acid construct, the nucleic acid construct comprising:

a) at least one glucose responsive protein 78 (grp78) non-coding regulatory sequence comprises a sequence from about 520 base pairs 5' of the site of initiation of transcription of the rat glucose responsive protein 78 (grp78) coding sequence to about 175 base pairs 3' of the site of initiation of the grp78 coding sequence; and

b) a heterologous nucleic acid sequence operatively linked to the regulatory sequence, wherein the heterologous sequence comprises a structural gene that encodes a biologically active protein that converts a non-therapeutically effective compound to a therapeutically-effective compound in vivo.